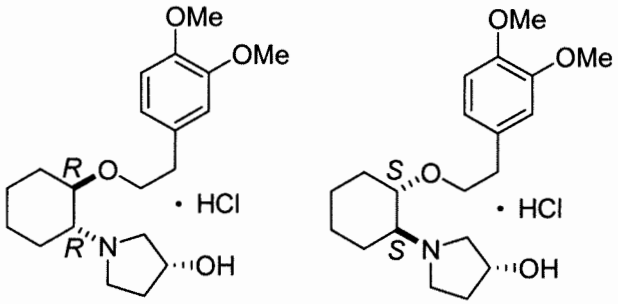
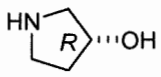
Claims

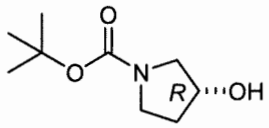
1. A method of making compound (1) or compound (2):



(1) or **(2)** ;

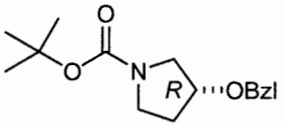
wherein the method comprises:

a) reacting  with $(Boc)_2O$ under suitable conditions to form compound (1R):



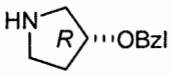
1R ;

b) reacting compound (1R) with benzyl bromide under suitable conditions to form compound (2R):

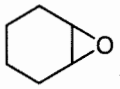


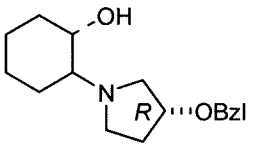
2R ;

c) hydrolyzing compound (2R) under suitable conditions to form compound (3R):

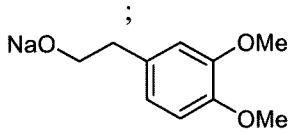


3R ;

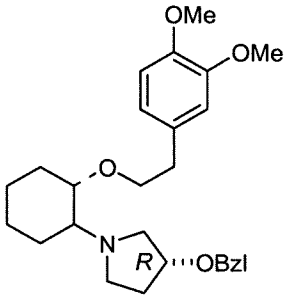
d) reacting compound (3R) with  under suitable conditions to form compound (4R):



4R ;

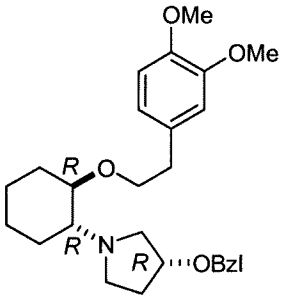


e) reacting compound (4R) with under suitable conditions to form compound (5R);

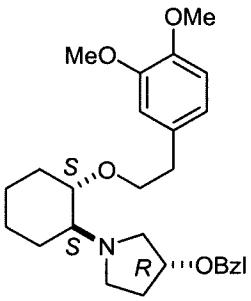


5R ;

f) resolving compound (5R) under suitable conditions to form compound (5RRR) and compound (5SSR):



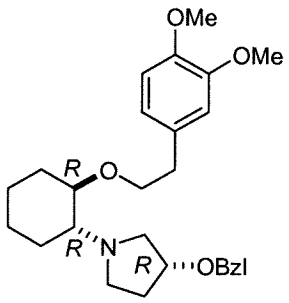
5RRR and

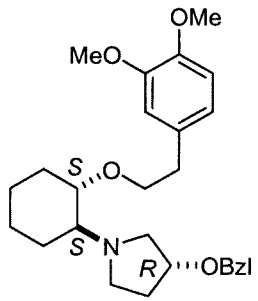


5SSR ; and

g) hydrogenolyzing compound (5RRR) under suitable conditions to form compound (1), as described above, and hydrogenolyzing compound (5SSR) under suitable conditions to form compound (2), as described above.

2. A method of making compound (5RRR) or compound (5SSR):



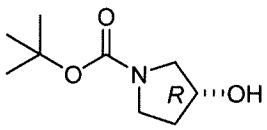
5RRR and 

5SSR ;

wherein the method comprises:

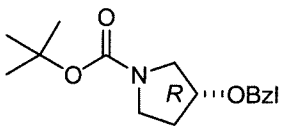
a) reacting 

with $(Boc)_2O$ under suitable conditions to form compound (1R):



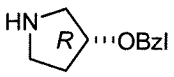
1R ;

b) reacting compound (1R) with benzyl bromide under suitable conditions to form compound (2R):

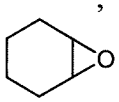


2R ;

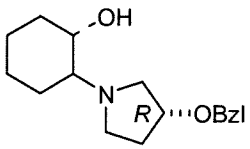
c) hydrolyzing compound (2R) under suitable conditions to form compound (3R):



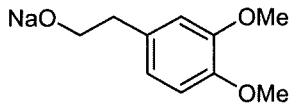
3R ;

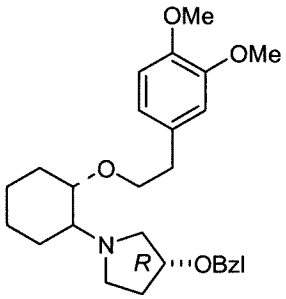
d) reacting compound (3R) with 

under suitable conditions to form compound (4R):



4R ;

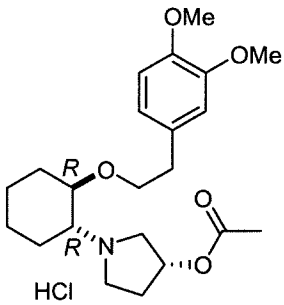
e) reacting compound (4R) with  under suitable conditions to form compound (5R);



5R ; and

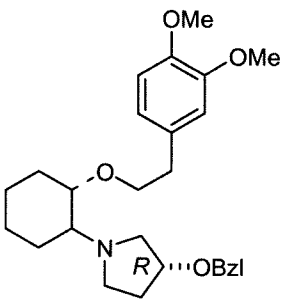
f) resolving compound (5R) under suitable conditions to form compound (5RRR) and compound (5SSR), as described above.

3. The method according to Claim 2 further comprising:
reacting compound (5RRR) under suitable conditions to form compound (17):



(17) .

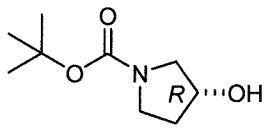
4. A method of making compound (5R):



5R ;

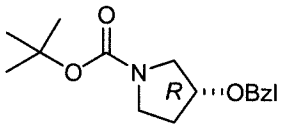
wherein the method comprises:

a) reacting  with $(Boc)_2O$ under suitable conditions to form compound (1R):



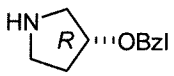
1R ;

b) reacting compound (1R) with benzyl bromide under suitable conditions to form compound (2R):

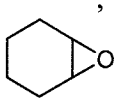


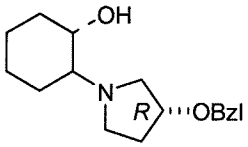
2R ;

c) hydrolyzing compound (2R) under suitable conditions to form compound (3R):

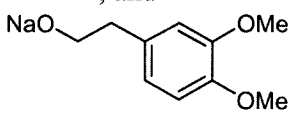


3R ;

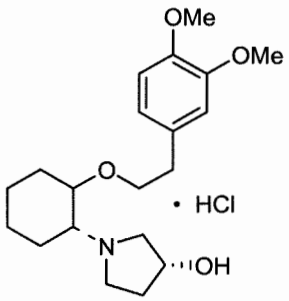
d) reacting compound (3R) with  under suitable conditions to form compound (4R):



4R ; and

e) reacting compound (4R) with  under suitable conditions to form compound (5R), as described above.

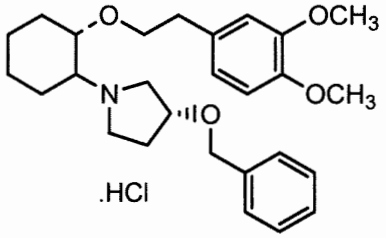
5. The method according to Claim 4 further comprising:
reducing compound (5R) under suitable conditions to form compound (4):



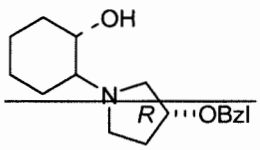
(4)

6. The method according to Claim 4 further comprising:

reacting compound (5R) under suitable conditions to form compound (12):



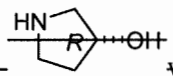
~~7. A method of making compound (4R):~~



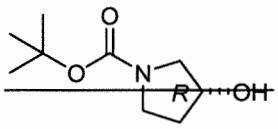
~~4R~~

;

~~wherein the method comprises:~~

~~a) reacting~~ 

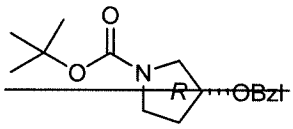
~~with $(Boc)_2O$ under suitable conditions to form compound (1R):~~



~~1R~~

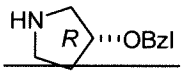
;

~~b) reacting compound (1R) with benzyl bromide under suitable conditions to form compound (2R):~~

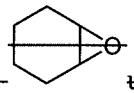


2R ;

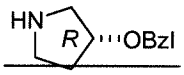
c) hydrolyzing compound (2R) under suitable conditions to form compound (3R):



3R ; and

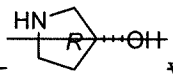
d) reacting compound (3R) with  under suitable conditions to form compound (4R), as described above.

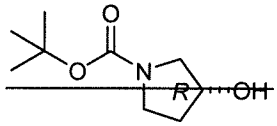
8. A method of making compound (3R):



3R ;

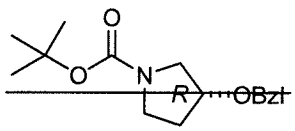
wherein the method comprises:

a) reacting  with $(Boc)_2O$ under suitable conditions to form compound (1R):



4R ;

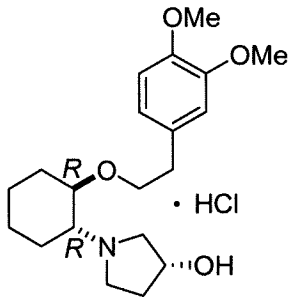
b) reacting compound (1R) with benzyl bromide under suitable conditions to form compound (2R):



2R ; and

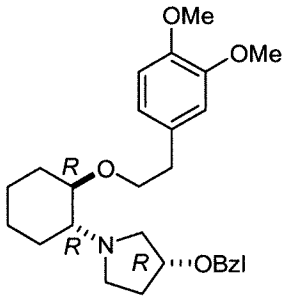
c) hydrolyzing compound (2R) under suitable conditions to form compound (3R), as described above.

~~9~~7. A method of making compound (1):



(1) ;

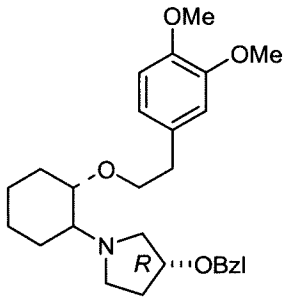
wherein the method comprises hydrogenolyzing compound (5RRR):



5RRR

under suitable conditions to form compound (1), as described above.

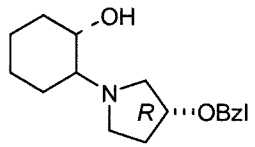
~~10~~8. The method according to claim ~~9~~7 further comprising, prior to the hydrogenolyzing step, resolving compound (5R):



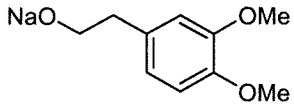
5R

under suitable conditions to form compound (5RRR), as described above.

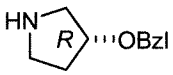
~~11~~9. The method according to claim ~~10~~8 further comprising, prior to the resolving step, reacting compound (4R):



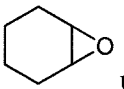
4R

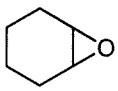
with  under suitable conditions to form compound (5R), as described above.

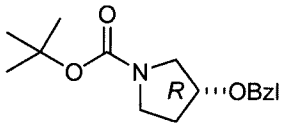
~~12~~10. The method according to claim ~~11~~ 9 further comprising, prior to the reacting step, reacting compound (3R):



3R

with  under suitable conditions to form compound (4R), as described above.

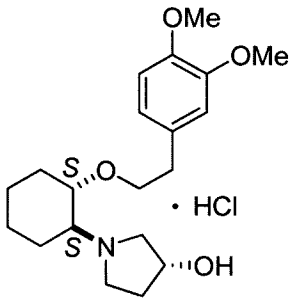
~~13~~11. The method according to claim ~~12~~ 10 further comprising, prior to the reaction of compound (3R) with , hydrolyzing compound (2R):



2R

under suitable conditions to form compound (3R), as described above.

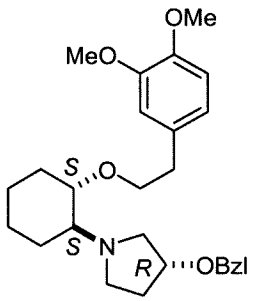
~~14~~12. A method of making compound (2):



(2)

;

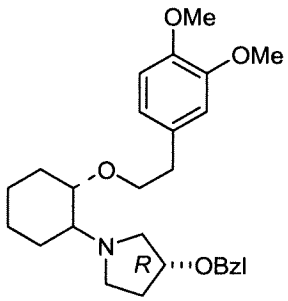
wherein the method comprises hydrogenolyzing compound (5SSR):



5SSR

under suitable conditions to form compound (2), as described above.

~~15~~13. The method according to claim ~~14~~12 further comprising, prior to the hydrogenolyzing step, resolving compound (5R):

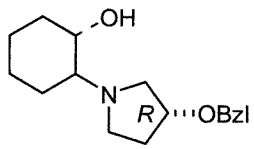


5R

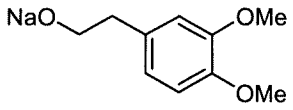
under suitable conditions to form compound (5SSR), as described above.

~~16~~14. The method according to claim ~~15~~13 further comprising, prior to the resolving step,

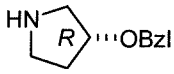
reacting compound (4R):



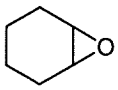
4R

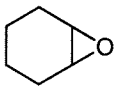
with  under suitable conditions to form compound (5R), as described above.

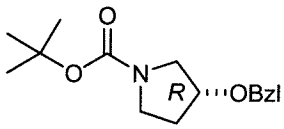
~~17~~15. The method according to claim ~~16~~ 14 further comprising, prior to the reacting step, reacting compound (3R):



3R

with  under suitable conditions to form compound (4R), as described above.

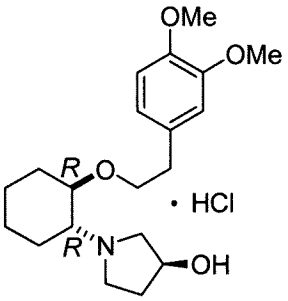
~~18~~16. The method according to claim ~~17~~ 15 further comprising, prior to the reaction of compound (3R) with , hydrolyzing compound (2R):



2R

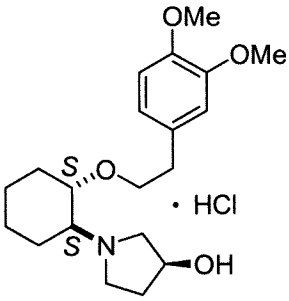
under suitable conditions to form compound (3R), as described above.

~~19~~17. A method of making compound (6) or compound (7):



(6)

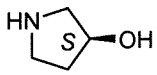
or



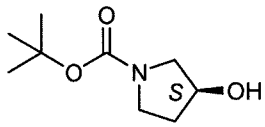
(7)

;

wherein the method comprises:

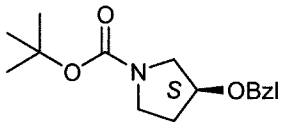
a) reacting 

with $(Boc)_2O$ under suitable conditions to form the following compound:



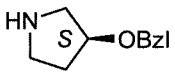
;

b) reacting the compound formed in step a) with benzyl bromide under suitable conditions to form the following compound:

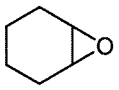


;

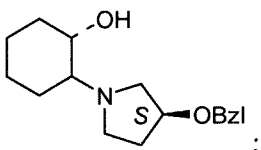
c) hydrolyzing the compound formed in step b) under suitable conditions to form the following compound:



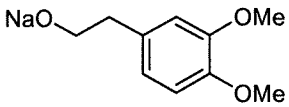
;

d) reacting the compound formed in step c) with 

under suitable conditions to form the following compound:

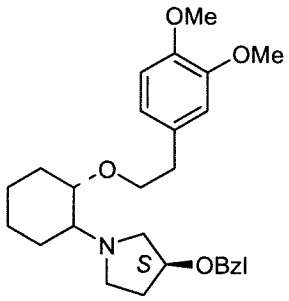


;

e) reacting the compound formed in step d) with 

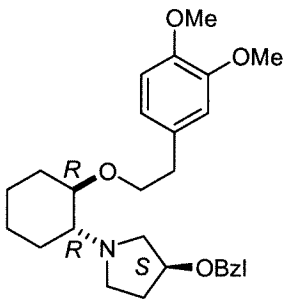
under

suitable conditions to form the following compound:

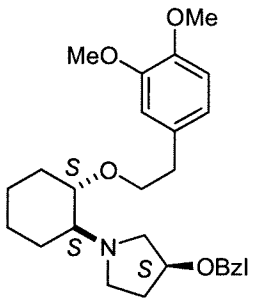


;

f) resolving the compound formed in step e) under suitable conditions to form the following compounds:

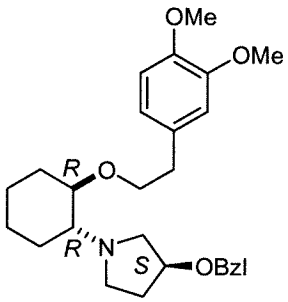


and



; and

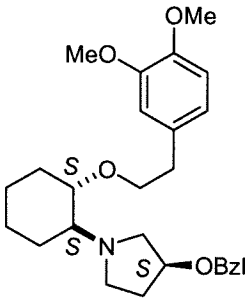
g) hydrogenolyzing the following compound formed in step f):



,

under suitable conditions to form compound (6), as described above;

and hydrogenolyzing the following compound formed in step f):

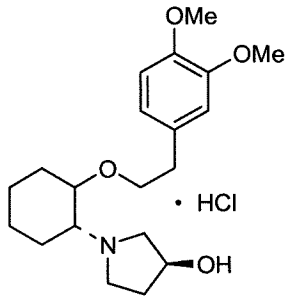


,

under suitable conditions to form compound (7), as described above.

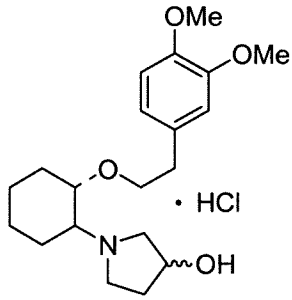
~~20~~18. The method according to claim ~~19~~ 17 further comprising:

reducing the compound formed in step e) under suitable conditions to form compound (5):



(5)

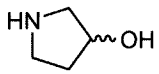
~~21~~19. A method of making compound (3):



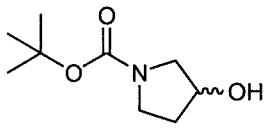
(3)

;

wherein the method comprises:

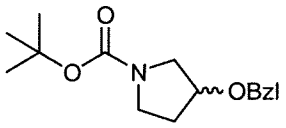
a) reacting 

with $(Boc)_2O$ under suitable conditions to form the following compound:



;

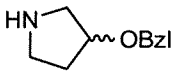
b) reacting the compound formed in step a) with benzyl bromide under suitable conditions to form the following compound:



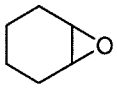
;

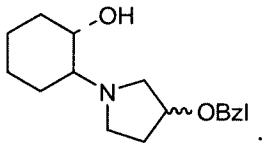
c) hydrolyzing the compound formed in step b) under suitable conditions to form the

following compound:

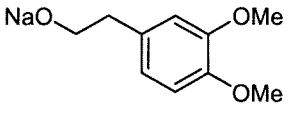


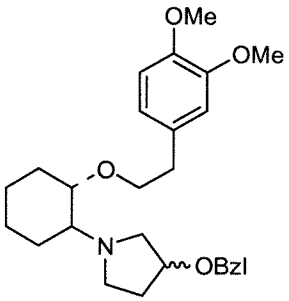
;

d) reacting the compound formed in step c) with  under suitable conditions to form the following compound:



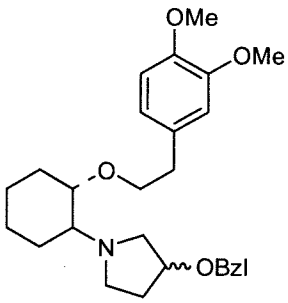
;

e) reacting the compound formed in step d) with  under suitable conditions to form the following compound:



;

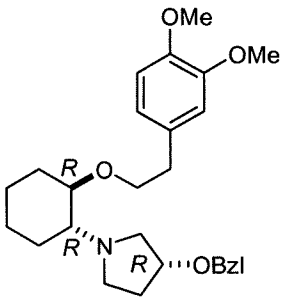
f) hydrogenolyzing the following compound formed in step e):



,

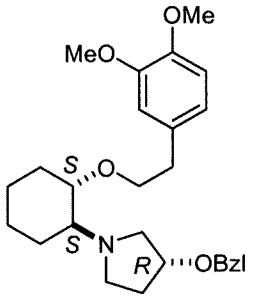
under suitable conditions to form compound (3), as described above.

~~22~~20. The compound (5RRR):



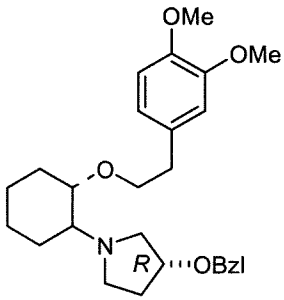
5RRR

~~23~~21. The compound (5SSR):



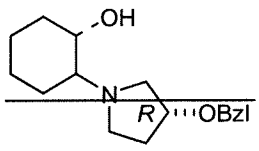
5SSR

~~24~~22. The compound (5R):



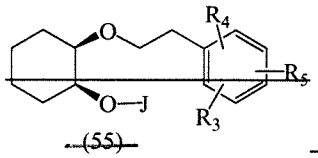
5R

~~25. The compound (4R):~~



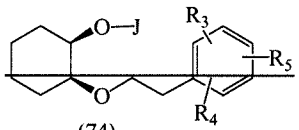
~~4R~~

~~26. A method of making a compound of formula (55) or formula (74):~~



(55)

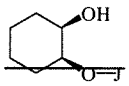
or



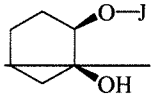
(74)

;

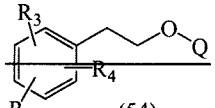
wherein the method comprises:



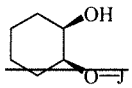
alkylating a compound of formula (53), (53) , or a compound of formula (84),



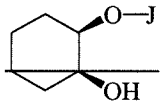
(84) , with a compound of formula (54),



(54) ; to form the compound of formula (55) or the compound of formula (74); respectively; and



optionally protecting a compound of formula (53), (53) , or a compound of formula



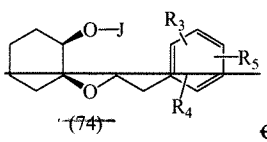
(84), (84) , before said alkylating step;

wherein O-Q is a leaving group that reacts with -OH in formula (53) or (84) to form the compound of formula (55) or the compound of formula (74), such that the stereochemical configuration of the compound of formula (53) or the compound of formula (84) is retained in the compound of formula (55) or the compound of formula (74), respectively;

wherein R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy, and C_1-C_6alkoxy, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen; and

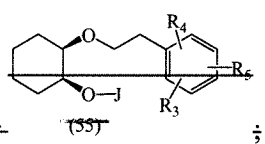
wherein O-J is a leaving group.

27. A method of making a compound of formula (74) or formula (55):



(74)

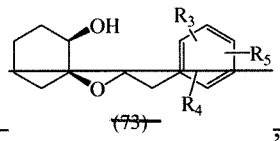
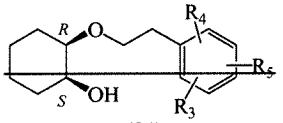
or



(55)

;

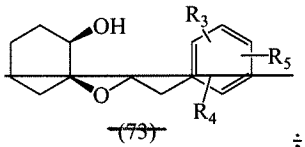
wherein the method comprises:

activating a compound of formula (73),  (73) , or a compound of formula (94),  (94) , with a hydroxy activating reagent to form the compound of formula (74) or the compound of formula (55), respectively;

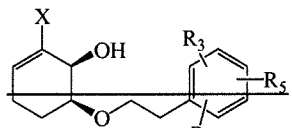
wherein R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy, and C_1-C_6alkoxy, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen; and

wherein O-J is a leaving group.

28. A method of making a compound of formula (73):


(73) ;

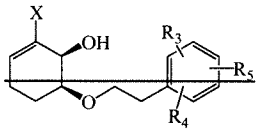
wherein the method comprises:


(72) , to form the compound of formula (73);

wherein X is a halide; and

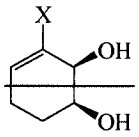
wherein R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy, and C_1-C_6alkoxy, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen.

29. A method of making a compound of formula (72):

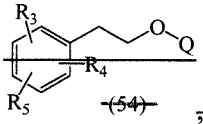


~~(72)~~ ;

~~wherein the method comprises:~~



~~alkylating a compound of formula (51),~~ ~~(51)~~ ~~, with a compound of formula (54),~~



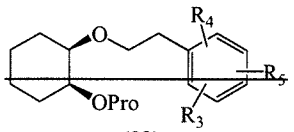
~~(54)~~ ~~, to form the compound of formula (72);~~

~~wherein X is a halide~~

~~wherein R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy, and C_1-C_6alkoxy, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen; and~~

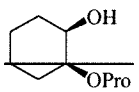
~~wherein O-Q is a leaving group that reacts with -OH in the compound of formula (51) to form the compound of formula (72), such that the stereochemical configuration of the compound of formula (51) is retained in the compound of formula (72).~~

~~30. A method of making a compound of formula (93):~~

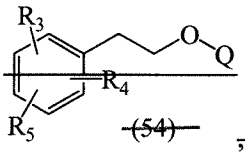


~~(93)~~ ;

~~wherein the method comprises:~~



~~alkylating a compound of formula (92),~~ ~~(92)~~ ~~, with a compound of formula (54),~~



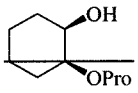
~~(54)~~ ~~, to form the compound of formula (93);~~

~~wherein Pro is a protecting group;~~

~~wherein R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy, and C_1-C_6alkoxy, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen; and~~

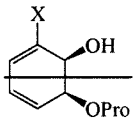
~~wherein O-Q is a leaving group that reacts with -OH in the compound of formula (92) to form the compound of formula (93), such that the stereochemical configuration of the compound of formula (92) is retained in the compound of formula (93).~~

~~31. A method of making a compound of formula (92):~~



~~(92)~~ ;

~~wherein the method comprises:~~

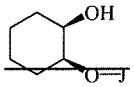


~~hydrogenating and hydrogenolyzing a compound of formula (91),~~ ~~(91)~~ ~~, to form the compound of formula (92);~~

~~wherein Pro is a protecting group; and~~

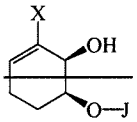
~~wherein X is a halide.~~

~~32. A method of making a compound of formula (53):~~



~~(53)~~ ;

~~wherein the method comprises:~~

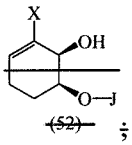


~~hydrogenating and hydrogenolyzing a compound of formula (52),~~ ~~(52)~~ ~~, to form the compound of formula (53);~~

~~wherein X is a halide; and~~

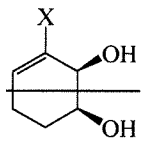
~~wherein O-J is a leaving group.~~

~~33. A method of making a compound of formula (52):~~



~~(52)~~ ;

~~wherein the method comprises:~~

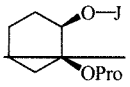


~~activating a compound of formula (51),~~ ~~(51)~~ ~~, with a hydroxy activating reagent to form the compound of formula (52);~~

~~wherein X is a halide; and~~

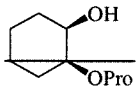
~~wherein O J is a leaving group.~~

~~34. A method of making a compound of formula (99):~~



~~(99)~~ ~~;~~

~~wherein the method comprises:~~

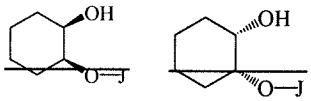


~~activating a compound of formula (92),~~ ~~(92)~~ ~~, with a hydroxy activating reagent to form the compound of formula (99);~~

~~wherein Pro is a protecting group; and~~

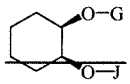
~~wherein O J is a leaving group.~~

~~35. A method of making a compound of formula (53) or a compound of formula (84):~~

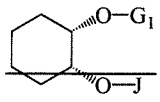


~~(53)~~ ~~or~~ ~~(84)~~ ~~;~~

~~wherein the method comprises:~~

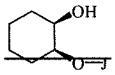


~~removing a functional group G or G_1 from a compound of formula (85),~~ ~~(85)~~ ~~, or a~~

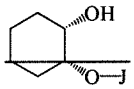


~~compound of formula (86),~~ ~~(86)~~ ~~, respectively, to form the compound of formula (53) or the compound of formula (84), respectively;~~

~~wherein O J is a leaving group.~~



~~36. A method comprising separating a racemic mixture of a compound of formula (53),~~ ~~(53)~~



~~and a compound of formula (84),~~ ~~(84)~~ ~~.~~

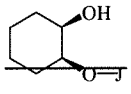
~~37. The method according to claim 36 wherein said separation step further comprises:~~

~~functionalizing one or both of the compound of formula (52) and the compound of formula (84) such that the compounds are capable of resolution;~~

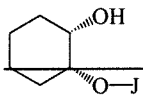
~~performing resolution to separate the compounds; and~~

~~optionally removing the functional group on said one or both functionalized compounds.~~

~~38. A method of forming a racemic mixture of a compound of formula (53) and a compound of formula (84):~~

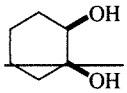


~~(53)~~ ~~and~~



~~(84)~~

~~wherein the method comprises:~~

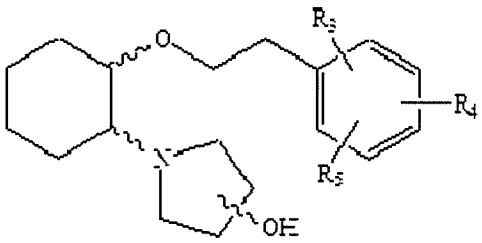


~~activating a compound of formula (83),~~ ~~(83)~~ ~~, with a hydroxy activating reagent to form the racemic mixture of the compound of formula (53) and the compound of formula (84);~~

~~wherein O-J is a leaving group.~~

~~39~~23. A compound of formula (IA), or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof:

(IA)



wherein, R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen.

4024. A compound of formula (IA) according to claim ~~39~~ 23, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

4125. A compound of formula (IA) according to claim ~~39~~ 23, or a solvate, pharmaceutically acceptable salt thereof, wherein, R_4 and R_5 are independently selected from hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

4226. A compound of formula (IA) according to claim ~~39~~ 23, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from hydroxy and C_1-C_6alkoxy.

4327. A compound of formula (IA) according to claim ~~39~~ 23, or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof, include.ing isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

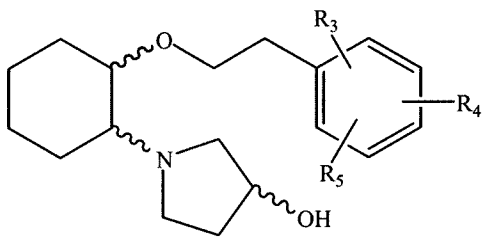
4428. A compound of formula (IA) according to claim ~~39~~ 23, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers

thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

4529. A compound of formula (IA) according to claim ~~39~~ 23, or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are C_1alkoxy.

4630. A compound of formula (IA) according to claim ~~39~~ 23, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are C_1alkoxy.

4731. A compound of formula (IB), or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof:



(IB)

wherein, R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen.

4832. A compound of formula (IB) according to claim ~~47~~ 31, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

4933. A compound of formula (IB) according to claim ~~47~~ 31, or a solvate, pharmaceutically acceptable salt thereof, wherein, R_4 and R_5 are independently selected from hydroxy and

C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~50~~34. A compound of formula (IB) according to claim ~~47~~ 31, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from hydroxy and C_1-C_6alkoxy.

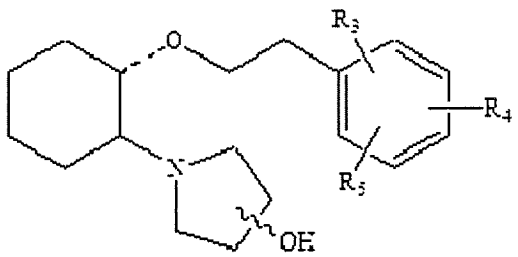
~~51~~35. A compound of formula (IB) according to claim ~~47~~ 31, or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

~~52~~36. A compound of formula (IB) according to claim ~~47~~ 31, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

~~53~~37. A compound of formula (IB) according to claim ~~47~~ 31, or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, metabolite, metabolic precursor or prodrug thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are C_1alkoxy.

~~54~~38. A compound of formula (IB) according to claim ~~47~~ 31, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are C_1alkoxy.

~~55~~39. A compound of formula (IC), or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof:



(IC)

wherein, R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen.

~~56~~40. A compound of formula (IC) according to claim ~~55~~ 39, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~57~~41. A compound of formula (IC) according to claim ~~55~~ 39, or a solvate, pharmaceutically acceptable salt thereof, wherein, R_4 and R_5 are independently selected from hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~58~~42. A compound of formula (IC) according to claim ~~55~~ 39, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from hydroxy and C_1-C_6alkoxy.

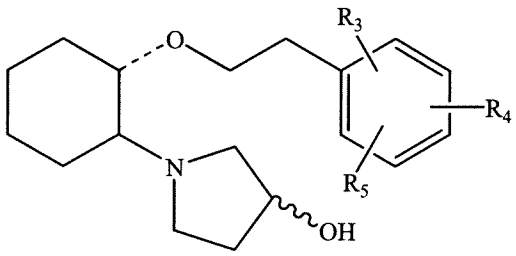
~~59~~43. A compound of formula (IC) according to claim ~~55~~ 39, or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

~~60~~44. A compound of formula (IC) according to claim ~~55~~ 39, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

~~61~~45. A compound of formula (IC) according to claim ~~55~~ 39, or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are C_1alkoxy.

~~62~~46. A compound of formula (IC) according to claim ~~55~~ 39, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_3 is hydrogen, R_4 and R_5 are C_1alkoxy.

~~63~~47. A compound of formula (ID), or a solvate, pharmaceutically acceptable salt, ester, amide,3complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof:



(ID)

wherein, R_3, R_4 and R_5 are independently selected from hydrogen, hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, with the proviso that R_3, R_4 and R_5 cannot all be hydrogen.

~~64~~48. A compound of formula (ID) according to claim ~~63~~ 47, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~65~~49. A compound of formula (ID) according to claim ~~63~~ 47, or a solvate, pharmaceutically acceptable salt thereof, wherein R_4 and R_5 are independently selected from hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~66~~50. A compound of formula (ID) according to claim ~~63~~ 47, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein R_3 is hydrogen, R_4 and R_5 are independently selected from hydroxy and C_1-C_6alkoxy.

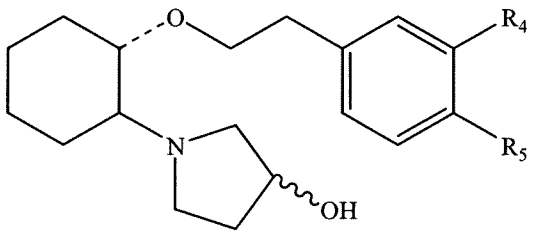
~~67~~51. A compound of formula (ID) according to claim ~~63~~ 47, or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein R_3 is hydrogen, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

~~68~~52. A compound of formula (ID) according to claim ~~63~~ 47, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein R_3 is hydrogen, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

~~69~~53. A compound of formula (ID) according to claim ~~63~~ 47, or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein R_3 is hydrogen, R_4 and R_5 are C_1alkoxy.

~~70~~54. A compound of formula (ID) according to claim ~~63~~ 47, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein R_3 is hydrogen, R_4 and R_5 are C_1alkoxy.

~~71~~55. A compound of formula (IE), or a solvate, pharmaceutically acceptable salt, ester, amide, complex, chelate, stereoisomer, stereoisomeric mixture, geometric isomer, crystalline or amorphous form, ~~metabolite,~~ metabolic precursor or prodrug thereof:



(IE)

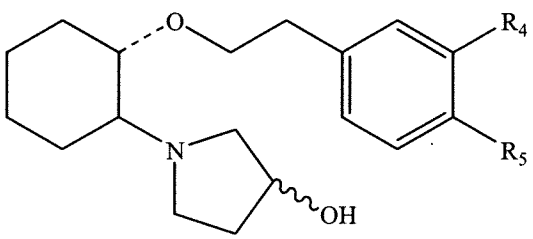
wherein, R_4 and R_5 are independently selected from hydrogen and hydroxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, with the proviso that R_4 and R_5 cannot all be hydrogen.

~~72~~56. A compound of formula (IE) according to claim ~~71~~ 55, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~73~~57. A compound of formula (IE) according to claim ~~71~~ 55, or a solvate, pharmaceutically acceptable salt thereof, wherein, R_4 and R_5 are independently hydroxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~74~~58. A compound of formula (IE) according to claim ~~71~~ 55, or a solvate, pharmaceutically acceptable salt thereof, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_4 and R_5 are independently hydroxy.

~~75~~59. A ~~metabolite,~~ metabolic precursor or prodrug of a compound of formula (IE):



(IE)

wherein, R_4 and R_5 are independently selected from hydrogen, hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, with the proviso that R_4 and R_5 cannot all be hydrogen.

~~76~~60. A ~~metabolite,~~ metabolic precursor or prodrug according to claim ~~75~~ 59, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~77~~61. A ~~metabolite,~~ metabolic precursor or prodrug according to claim ~~75~~ 59, wherein, R_4 and R_5 are independently selected from hydroxy and C_1-C_6alkoxy, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof.

~~78~~62. A ~~metabolite,~~ metabolic precursor or prodrug according to claim ~~75~~ 59, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_4 and R_5 are independently selected from hydroxy and C_1-C_3alkoxy.

~~79~~63. A ~~metabolite,~~ metabolic precursor or prodrug according to claim ~~75~~ 59, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_4 and R_5 are independently selected from C_1-C_6alkoxy.

~~80~~64. A ~~metabolite,~~ metabolic precursor or prodrug according to claim ~~75~~ 59, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_4 and R_5 are independently selected from C_1-C_3alkoxy.

~~81~~65. A ~~metabolite,~~ metabolic precursor or prodrug according to claim ~~75~~ 59, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_4 and R_5 are C_1alkoxy.

~~82~~66. A ~~metabolite,~~ metabolic precursor or prodrug according to claim ~~75~~ 59, including isolated enantiomeric, diastereomeric and geometric isomers thereof, and mixtures thereof, wherein, R_4 and R_5 are C_1alkoxy.

~~83~~67. A composition comprising: a compound according to any one of claims ~~39 to 74~~23 to 58 or a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, in combination with a pharmaceutically acceptable carrier, excipient or diluent.

~~84~~68. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament.

~~85~~69. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for modulating ion channel activity in a warm-blooded animal.

~~86~~70. A method for modulating ion channel activity in an *in vitro* setting comprising administering *in vitro* an effective amount of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, a composition according to claim ~~83~~ 67, or a medicament manufactured according to claim ~~84~~ 68.

~~87~~71. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for blocking/inhibiting the activity/conductance of an ion channel in a warm-blooded animal.

~~88~~72. A method for blocking/inhibiting the activity/conductance of an ion channel in an *in vitro* setting comprising administering *in vitro* an effective amount of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, or a medicament manufactured according to claim ~~84~~ 68.

~~89~~73. The use according to claim ~~85 or 87~~ 69 or 71, wherein said ion channel is a potassium channel.

~~90~~74. The use according to claim ~~89~~ 73, wherein said potassium channel is a voltage-activated potassium channel.

~~91~~75. The method according to claim ~~86 or 88~~ 70 or 72, wherein said ion channel is a potassium channel.

~~92~~76. The method according to claim ~~91~~ 75, wherein said potassium channel is a voltage-activated potassium channel.

~~93~~77. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for modulating cardiac early repolarising currents and cardiac sodium currents in a warm-blooded animal.

~~94~~78. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for blocking/inhibiting cardiac early repolarising currents and cardiac sodium currents in a warm-blooded animal.

~~95~~79. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for blocking/inhibiting the cardiac ion channels responsible for the cardiac early repolarising currents and cardiac sodium currents in a warm-blooded animal.

~~96~~80. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for blocking/inhibiting cardiac early repolarising currents and cardiac sodium currents in a warm-blooded animal under conditions where an arrhythmogenic substrate is present in the heart of said warm-blooded animal.

~~97~~81. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic

precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for blocking/inhibiting the cardiac ion channels responsible for the cardiac early repolarising currents and cardiac sodium currents in a warm-blooded animal under conditions where an arrhythmogenic substrate is present in the heart of said warm-blooded animal.

~~98~~82. The use according to any one of claims ~~93 to 97~~ 77 to 81, wherein said cardiac early repolarising currents comprise ionic currents which activate rapidly after depolarisation of membrane voltage and which effect repolarisation of the cell.

~~99~~83. The use according to any one of claims ~~93 to 97~~ 77 to 81, wherein said early repolarising currents comprise the cardiac transient outward potassium current (I_{to}) and/or the ultrarapid delayed rectifier current (I_{Kur}).

~~100~~84. The use according to claim ~~99~~ 83, wherein the cardiac transient outward potassium current (I_{to}) and/or the ultrarapid delayed rectifier current (I_{Kur}) comprise at least one of the Kv4.2, Kv4.3, Kv2.1, Kv1.4 and Kv1.5 currents.

~~101~~85. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating and/or preventing arrhythmia in a warm-blooded animal.

~~102~~86. A pharmaceutical composition comprising an amount of a compound according to any one of claims ~~39 to 74~~ 23 to 58, or a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66 , effective to treat and/or prevent atrial arrhythmia in a warm-blooded animal in need of the treatment and/or prevention, and a pharmaceutically acceptable carrier, diluent, or excipient.

~~103~~87. Use of a compound according to any one of claims ~~39 to 74~~23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating and/or preventing atrial arrhythmia in a warm-blooded animal.

~~104~~88. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating and/or preventing ventricular arrhythmia in a warm-blooded animal.

~~105~~89. A pharmaceutical composition comprising an amount of a compound according to any one of claims ~~39 to 74~~ 23 to 58, or a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, effective to treat and/or prevent ventricular arrhythmia in a warm-blooded animal in need of the treatment and/or prevention, and a pharmaceutically acceptable carrier, diluent, or excipient.

~~106~~90. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating and/or preventing atrial fibrillation in a warm-blooded animal.

~~107~~91. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating and/or preventing atrial flutter in a warm-blooded animal.

~~108~~92. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating and/or preventing ventricular fibrillation in a warm-blooded animal.

~~109~~93. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating and/or preventing ventricular flutter in a warm-blooded animal.

~~110~~94. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a

composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating atrial fibrillation in a warm-blooded animal.

~~111~~95. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating atrial flutter in a warm-blooded animal.

~~112~~96. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating ventricular fibrillation in a warm-blooded animal.

~~113~~97. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for treating ventricular flutter in a warm-blooded animal.

~~114~~98. Use of a compound according to any one of claims ~~39 to 74~~23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for preventing atrial fibrillation in a warm-blooded animal.

~~115~~99. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for preventing atrial flutter in a warm-blooded animal.

~~116~~100. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for preventing ventricular fibrillation in a warm-blooded animal.

~~117~~101. Use of a compound according to any one of claims ~~39 to 74~~ 23 to 58, a ~~metabolite,~~ metabolic precursor or prodrug according to any one of claims ~~75 to 82~~ 59 to 66, or a composition according to claim ~~83~~ 67, in the manufacture of a medicament for preventing ventricular flutter in a warm-blooded animal.